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Published in:
Journal of the American College of Cardiology

DOI:
10.1016/j.jacc.2015.06.1314

Publication date:
2015

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER INC.

VOL. 66, NO. 9, 2015
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2015.06.1314

Incidence of Atrial Fibrillation and Relationship With Cardiovascular Events, Heart Failure, and Mortality

A Community-Based Study From the Netherlands

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ABSTRACT

BACKGROUND Important improvements have been made in treatment of diseases associated with atrial fibrillation (AF), such as hypertension, myocardial infarction, and heart failure. Incidence rates and risk factors may have changed with the aging of the population and changing lifestyles. Currently, the risk for AF is only partially explained, possibly because of differences between older cohorts and contemporary populations.

OBJECTIVES This study investigated the incidence of AF in a contemporary cohort in the Netherlands, together with comorbidities associated with AF and associations of AF with cardiovascular outcomes.

METHODS Incident AF was ascertained for hospital and study electrocardiograms in 8,265 participants of the PREVEND (Prevention of Renal and Vascular End-Stage Disease) study in Groningen, the Netherlands.

RESULTS During 9.7 ± 2.3 years of follow-up, 265 participants developed AF, with a resulting overall AF incidence of 3.3 per 1,000 person-years. Advancing age, male sex, antihypertensive drug use, higher body mass index, previous myocardial infarction, and previous stroke were associated with AF. After multivariable adjustment, AF was associated with cardiovascular events (hazard ratio [HR]: 2.24; 95% confidence interval [CI]: 1.06 to 4.75; $p = 0.035$), heart failure with either reduced or preserved ejection fraction (HR: 4.52; 95% CI: 2.02 to 10.09; $p < 0.001$), and all-cause mortality (HR: 3.02; 95% CI: 1.73 to 5.27; $p < 0.001$).

CONCLUSIONS The incidence of AF in the present cohort was comparable to that shown in data of older studies. Obesity has become a major risk factor for incident AF. Although overall cardiovascular event rates were lower in the present study, the present study confirms the association of incident AF with such events. (J Am Coll Cardiol 2015;66:1000–7)

Atrial fibrillation (AF) affects millions of people worldwide, and numbers are expected to increase (1). AF has large impact on a person's life. It is accompanied by symptoms, impaired quality of life, increased risk of stroke, dementia, heart failure, mortality, and increasing health care expenses (2,3).

Multiple comorbidities have been associated with incident AF (4). However, current knowledge of AF

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Manuscript received June 8, 2015; accepted June 22, 2015.

incidence, prevalence, risk factors, and associated cardiovascular morbidity and mortality is derived from predominantly North American cohort studies that were initiated a long time ago or, more recently, from registries based on questionnaires or International Classification of Diseases (ICD) discharge codes (5-10). In recent years, important improvements were made in pharmacological and nonpharmacological treatment of associated diseases, such as hypertension, myocardial infarction, and heart failure (11-13). In addition, incidence rates and risk factors may have changed with the aging of the population and changing lifestyles. Currently, the risk for incident AF is only partially explained, possibly because of differences between older cohorts and more contemporary populations. We investigated the incidence of AF, comorbidities associated with AF, and the associations of AF with cardiovascular events, systolic and diastolic heart failure, and all-cause mortality in the Dutch community-based PREVEND (Prevention of Renal and Vascular End-Stage Disease) cohort study.

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METHODS

POPULATION. The PREVEND cohort study was founded in 1997 by inviting all inhabitants of the city of Groningen, the Netherlands, who were 28 to 75 years old (n = 85,421) (14). Of all invitees, 40,856 responded (47.8%). Persons with urinary albumin excretion >10 mg/l (n = 7,768) in their morning urine, as well as a randomly selected control group with urinary albumin excretion <10 mg/l (n = 3,394), were invited to the PREVEND outpatient clinic. After excluding patients with insulin-dependent diabetes mellitus, pregnant women, and persons unable or unwilling to participate, a final cohort of 8,592 patients was included and completed the baseline screening program. The baseline screening program consisted of 2 outpatient visits to assess demographic factors, anthropometric measurements, cardiovascular and metabolic risk factors, and health behavior and to collect blood samples and 2 24-h urine samples on 2 consecutive days. Participants were seen at 3-year intervals in the PREVEND outpatient clinic. For the present analysis, we excluded participants without an electrocardiogram (ECG) (n = 248), as well as participants with prevalent AF at the baseline screening (n = 79), thus leaving 8,265 participants. The PREVEND study was approved by the institutional medical ethics committee and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

ASSESSMENT OF AF. Incident AF was diagnosed if either atrial flutter or AF was present on a 12-lead ECG obtained at 1 of the 3 PREVEND follow-up visits or at an outpatient visit or hospital admission in the 2 hospitals in the city of Groningen (University Medical Center Groningen and Martini Hospital). A standard 12-lead ECG was performed at each PREVEND follow-up visit. All ECGs were digitally stored and electronically screened for the following criteria: PR interval absence, atrial flutter, or ectopic atrial rhythm. This method of electronic screening was validated with complete manual screening by 2 independent observers of all ECGs from the PREVEND baseline visit, and 100% sensitivity for the detection of AF or atrial flutter was reached. All ECGs determined by electronic screening to suggest suspected AF were manually reviewed by 2 independent observers. When an inconsistency was found or when both observers agreed on the diagnosis of AF or atrial flutter, the ECGs were validated by 2 independent cardiologists (Figure 1). Incident AF was diagnosed in 265 participants. For the date of incident AF, the date of the first ECG with a definite diagnosis of AF or atrial flutter was used.

COVARIATE DEFINITIONS. Systolic and diastolic blood pressures were calculated as the mean of the last 2 measurements of the 2 visits, by using an

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

BMI = body mass index

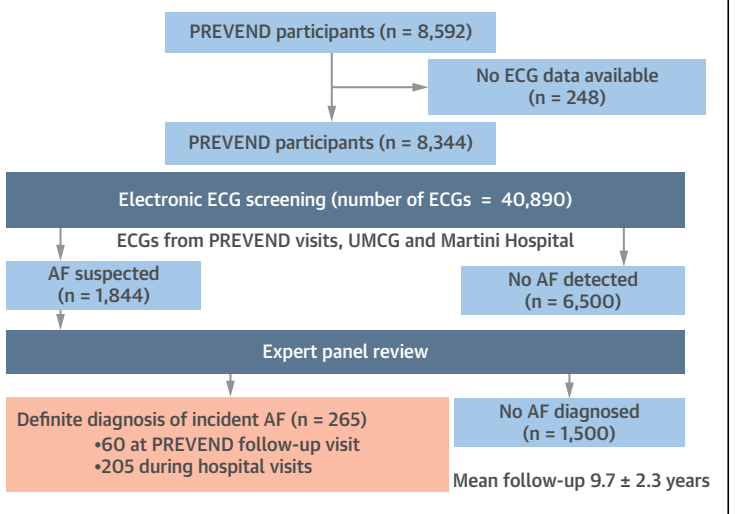
ECG = electrocardiogram

ICD = International Classification of Diseases

LVEF = left ventricular ejection fraction

NT-proBNP = N-terminal prohormone of brain natriuretic peptide

FIGURE 1 AF Ascertainment in the PREVEND Study



Flowchart of atrial fibrillation (AF) assessment in PREVEND (Prevention of Renal and Vascular End-Stage Disease) study participants, by using electrocardiograms (ECGs) made during PREVEND study visits and hospital visits. UMCG = University Medical Center Groningen.

TABLE 1 Participants' Characteristics

	Incident AF (n = 265)	No AF (n = 8,000)	p Value
Age, yrs	62 ± 9	49 ± 13	<0.001
Male	185 (70)	3,935 (49)	<0.001
Caucasian	252 (95)	7,592 (95)	1.000
BMI, kg/m^2	28 ± 4	26 ± 4	<0.001
Obesity	61 (23)	1,226 (15)	0.001
Systolic blood pressure, mm Hg	143 ± 23	129 ± 20	<0.001
Diastolic blood pressure, mm Hg	78 ± 10	74 ± 10	<0.001
Heart rate, bpm	67 ± 11	69 ± 10	0.002
Antihypertensive drug use	99 (37)	999 (12)	<0.001
Hypertension	145 (54)	2,092 (26)	<0.001
Previous myocardial infarction	41 (15)	210 (3)	<0.001
Heart failure	6 (2.3)	12 (0.2)	<0.001
Diabetes mellitus	23 (9)	287 (4)	<0.001
Previous stroke	7 (2.6)	50 (0.6)	0.002
Peripheral artery disease	28 (11)	263 (3)	<0.001
Smoking	97 (37)	3,573 (45)	0.012
Alcohol consumption	31 (12)	1,023 (13)	0.641
Hypercholesterolemia	35 (13)	326 (4)	<0.001
PR interval duration, ms	168 (153–187)	158 (143–172)	<0.001
eGFR, ml/min	75 (68–84)	80 (72–90)	<0.001
UAE, mg/24 h	16 (8–39)	9 (6–17)	<0.001
NT-proBNP, ng/l	103 (44–248)	36 (16–70)	<0.001
Highly sensitive CRP, mg/l	2.0 (0.8–3.6)	1.3 (0.6–2.9)	<0.001

Values are mean ± SD, n (%), or median (interquartile range).

AF = atrial fibrillation; BMI = body mass index; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; NT-proBNP = N-terminal prohormone of brain natriuretic peptide; UAE = 24-h urine albumin excretion.

automatic Dinamap XL Model 9300 series device (Johnson & Johnson Medical Inc., Tampa, Florida). Hypertension was defined as systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or use of antihypertensive drugs. Body mass index (BMI) was calculated as the ratio of weight to height squared (kg/m^2), and obesity was defined as a BMI >30 kg/m^2. Type 2 diabetes was defined as a fasting plasma glucose >7.0 mmol/l (126 mg/dl), a nonfasting plasma glucose >11.1 mmol/l, or use of antidiabetic drugs. Urinary albumin excretion was calculated as the average value from 2 consecutive 24-h urine collections. The estimated glomerular filtration rate was estimated using the simplified modification of diet in renal disease formula. Smoking was defined as current nicotine use or having stopped smoking within the previous 5 years. Hypercholesterolemia was defined as total serum cholesterol >6.5 mmol/l (251 mg/dl), serum total cholesterol ≥5.0 mmol/l (193/mg/dl) if a history of myocardial infarction was present, or use of lipid-lowering drugs. Alcohol consumption was defined as 4 alcoholic drinks/day or more in men and 1 to 3 alcoholic drinks/day or more in women. History of myocardial infarction or stroke was defined as participant-reported hospitalization for at least 3 days as a result of this condition. Peripheral artery disease was defined as an ankle-brachial index <0.9. A committee of experts in heart failure adjudicated all participants with heart failure at baseline according to previously published criteria (14). N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and highly sensitive C-reactive protein were measured as described previously (15,16).

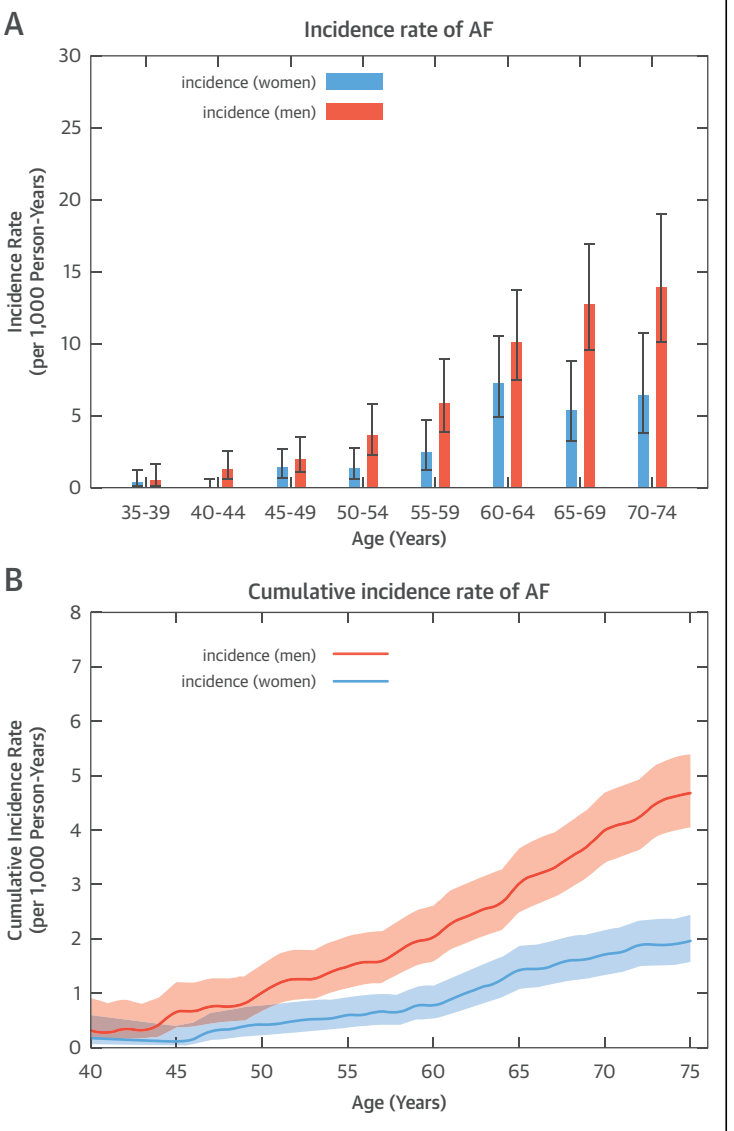
FOLLOW-UP. The follow-up duration was calculated as the time between the baseline screening visit and the last contact date, death, or December 31, 2008 (end of the third PREVEND follow-up visit), whichever came first.

CARDIOVASCULAR EVENTS, HEART FAILURE, AND ALL-CAUSE MORTALITY ASSESSMENT. Information on cardiovascular events was obtained from PRISMANT, the Dutch national registry of hospital discharge diagnoses. The validity of this database has been confirmed before, with 84% of primary diagnoses and 87% of secondary diagnoses matching the diagnoses recorded in participants' charts (17). Use of hospital discharge diagnoses and government vital statistics was part of the original study design (18). Data were coded according to the 10th revision of the ICD. Cardiovascular events consisted of cardiac events (acute myocardial infarction [ICD code 410], acute and subacute ischemic heart disease [ICD 411], coronary artery bypass grafting or percutaneous transluminal coronary angioplasty), cerebrovascular events (occlusion or stenosis of the precerebral [ICD 433] or cerebral arteries [ICD 434], subarachnoid hemorrhage [ICD 430]), and peripheral events (other vascular interventions such as percutaneous transluminal angioplasty or bypass grafting of the aorta and peripheral vessels). A committee of experts on heart failure adjudicated all incident heart failure events according to previously published criteria and categorized these events, on the basis of the left ventricular ejection fraction (LVEF) and diastolic dysfunction, into either heart failure with reduced ejection fraction (LVEF <40%) or heart failure with preserved ejection fraction (LVEF >50%) (14). Six participants with heart failure had an LVEF of 41% to 49%. These patients were included in the total number of patients with heart failure but were not involved in analyses specific for this group because of the low number of events. There was no classification made on the basis of underlying cause because many patients with heart failure have more than one comorbidity. Data on mortality were obtained through the municipal registration. Cause of death was ascertained by linking the number of the

death certificate to the primary cause of death as coded by the Dutch Central Bureau of Statistics. Information on dates and causes of death for every participant was obtained from Statistics Netherlands (19), according to the 10th revision of the ICD.

STATISTICAL ANALYSIS. We used a statistical weighting method to adjust for the oversampling of patients with microalbuminuria at the study's start and to allow generalization of results to the general population (16). Participants' characteristics were presented as mean ± SD or median (range) for continuous variables and counts with percentages for categorical variables. Incidence rates for the number of AF cases or outcome events per 1,000 person-years of observation and 95% confidence intervals (95% CIs) were calculated (20). We estimated multivariable Cox proportional hazards regression models to assess risk factors for incident AF during follow-up; death was considered a censoring event. We examined the proportionality assumption by calculating the Schoenfeld residuals and by plotting the scaled Schoenfeld residuals against time. There were no violations of the proportional hazards assumption. We selected risk factors for the incident AF analyses on the basis of earlier reports and availability in clinical practice (11,12). Age- and sex-adjusted covariates with a $p < 0.1$ were stepwise incorporated in a multivariable-adjusted model, with the order based on the highest Wald statistic. The final multivariable model included all covariates with $p < 0.05$. Finally, interactions in the multivariate model were tested. In view of multiple testing, we applied a Bonferroni correction to the interaction analysis, to minimize false-positive findings. Population-attributable risks for reversible or treatable risk factors in the multivariate model were calculated using the following formula: ([total AF incidence rate − unexposed AF incidence rate] / [total AF incidence rate]) × 100% (21). We used Cox time-dependent regression analyses, with AF as time-varying covariate to study the association of incident AF and future cardiovascular events, heart failure, and all-cause mortality. We adjusted for clinically significant covariates, on the basis of earlier publications (22–24). In Model 1 we adjusted for age and sex, and in Model 2 we adjusted for age, sex, heart failure, antihypertensive drug use, diabetes, previous stroke, previous myocardial infarction, peripheral artery disease, and NT-proBNP. All analyses were performed using R package (version 3.0.3; R Foundation for Statistical Computing, Vienna, Austria), and a 2-tailed p value <0.05 was considered statistically significant.

FIGURE 2 AF Incidence in the PREVEND Study



(A) Incidence rate of atrial fibrillation (AF) as a function of age for men and women. The 95% confidence intervals are shown using **error bars**. **(B)** Cumulative incidence rate of AF as a function of age for men and women. The **salmon line** is the (smoothed) cumulative incidence rate curve for men; the **blue line** is the cumulative incidence rate curve for women. The 95% confidence intervals are shown using **shaded areas**. The cumulative incidence rate at a given age is the incidence rate of atrial fibrillation in the group of all people younger than the given age. Incidence rates are per 1,000 person-years of follow-up. PREVEND = Prevention of Renal and Vascular End-Stage Disease.

RESULTS

PARTICIPANTS' CHARACTERISTICS. The mean age of PREVEND participants was 49 ± 13 years, and 49.8% were men. Total follow-up duration of 8,265 PREVEND participants was 80,352 person-years. During a mean follow-up of 9.7 ± 2.3 years, 265

(80 women, 185 men) participants (3%) developed AF (AF incidence rate: 3.3 per 1,000 person-years; 95% CI: 3.0 to 3.8) (Table 1). Participants with incident AF were 62 ± 9 years of age, and 70% were men. Of the 265 participants with incident AF, 60 (23%) received the diagnosis at a PREVEND visit, and the other 205 (77%) received the diagnosis at a hospital visit or admission. Both cumulative and noncumulative incidence rates for incident AF stratified by age and sex demonstrated higher AF incidence rates in older persons (Figures 2A and 2B). The primary comorbidities in participants with incident AF were hypertension (54%), obesity (23%), and previous myocardial infarction (15%).

RISK FACTORS OF INCIDENT AF. Age- and sex-adjusted analyses revealed that higher BMI, higher systolic blood pressure, antihypertensive drug use, previous myocardial infarction, heart failure, previous stroke, lower heart rate, and higher NT-proBNP were associated with an increased risk of incident AF (Table 2). After stepwise addition of covariates, the final multivariable model consisted of 6 covariates (Central Illustration): advancing age, male sex, BMI, antihypertensive drug use, previous myocardial infarction, and previous stroke. There were no significant interactions in the multivariate model. Population-attributable risk estimates for the most significant reversible or treatable risk factors for incident AF were calculated: the risk factor that contributed most to incident AF in the present population was antihypertensive drug use (32%), followed by previous myocardial infarction (16%), obesity (9%), and previous stroke (3%).

ASSOCIATIONS OF AF WITH CARDIOVASCULAR EVENTS, HEART FAILURE, AND ALL-CAUSE MORTALITY. Incidence rates of cardiovascular outcomes for participants with and without incident AF are described in Table 3. The incidence of cardiovascular events in participants with AF was higher compared with participants without AF (incidence rate per 1,000 person-years: 20.59; 95% CI: 14.84 to 28.64 vs. 10.13; 95% CI: 9.43 to 10.87, respectively; hazard ratio [HR]: 1.97; 95% CI: 1.24 to 3.13). Cardiac events were most common, followed by cerebrovascular and peripheral events. The incidence rate per 1,000 person-years of heart failure after diagnosis of AF was 18.14 (95% CI: 13.19 to 25.01), compared with 2.91 (95% CI: 2.55 to 3.31) in participants without AF (HR: 6.01; 95% CI: 2.83 to 12.76). Heart failure with reduced ejection fraction was more common than heart failure with preserved ejection fraction. The incidence rate per 1,000 person-years of all-cause mortality after diagnosis of AF was 28.96 (95% CI: 23.05 to 36.42), compared with 6.84 (95% CI: 6.28 to 7.44) in participants without AF (HR: 4.14; 95% CI: 2.64 to 6.51). Incident AF was associated with cardiovascular events (multivariable adjusted HR: 2.24; 95% CI: 1.06 to 4.75; $p = 0.035$), with heart failure (multivariable adjusted HR: 4.52; 95% CI: 2.02 to 10.09; $p < 0.001$), and with all-cause mortality (multivariable adjusted HR: 3.02; 95% CI: 1.73 to 5.27; $p < 0.001$) (Table 4). Incident AF was associated with both heart failure with reduced ejection fraction (multivariable adjusted HR: 4.00; 95% CI: 1.49 to 10.73; $p = 0.006$) and heart failure with preserved ejection fraction (multivariable adjusted HR 6.82; 95% CI: 2.47 to 18.79; $p < 0.001$).

TABLE 2 Age- and Sex-Adjusted Cox Proportional Hazards Models for Determinants of Incident AF

Covariate	Hazard Ratio (95% CI)	p Value
BMI, per 5 kg/m^2	1.45 (1.21–1.74)	<0.001
Systolic blood pressure, per 10 mm Hg	1.11 (1.01–1.22)	0.025
Heart rate, per 5 bpm	0.89 (0.81–0.98)	0.022
Antihypertensive drug use	2.14 (1.43–3.20)	<0.001
Previous myocardial infarction	2.56 (1.51–4.35)	<0.001
Heart failure	2.72 (1.06–6.97)	0.037
Previous stroke	4.63 (1.50–14.26)	0.008
NT-proBNP (per 1,000 ng/l)	1.08 (1.07–1.10)	<0.001

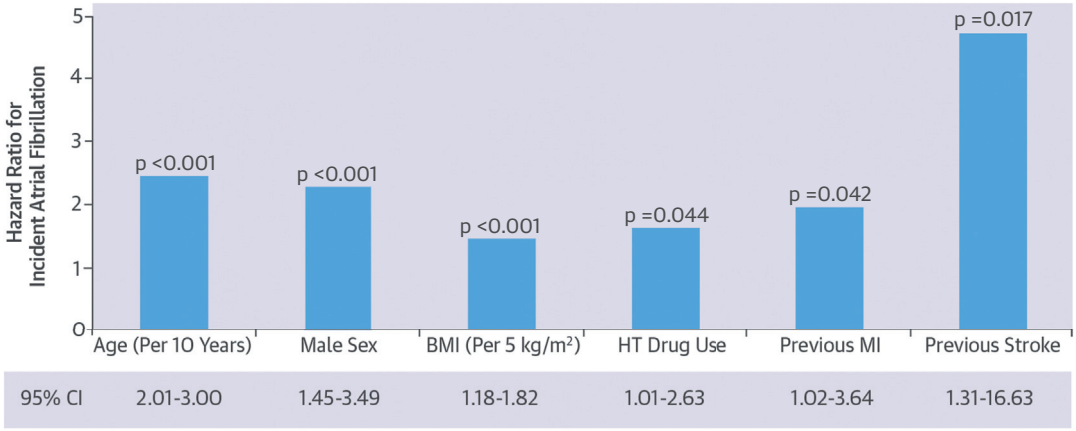
CI = confidence interval; other abbreviations as in Table 1.

DISCUSSION

The present contemporary community-based study in the Netherlands had 3 primary findings. First, the AF incidence in the present population was 3.3 per 1,000 person-years, comparable to that in older epidemiological studies. Second, in addition to the conventional risk factors for AF, BMI was strongly associated with AF. Third, we confirmed that AF, despite lower overall event rates, is associated with an adverse outcome.

INCIDENCE OF AF. In the present study, we identified 265 participants with incident AF, and the overall incidence rate of AF was 3.3 per 1,000 person-years. AF incidence was higher in men than in women, and there was a strong increase with age that is comparable to other studies (5–8,25). The incidence is lower than observed in the Rotterdam Study, also from the Netherlands, in which the overall incidence rate of AF was 9.9 per 1,000 person-years. This variation is probably caused by the age difference of included participants (in Rotterdam, >55 years; in PREVEND, between 28 and 75 years) (25). Many of the epidemiological studies on AF—the Olmsted County study (AF documented from 1980 to 2000) (8), the

CENTRAL ILLUSTRATION **AF in a Community-Based Cohort in the Netherlands: Multivariate Determinants of Incident AF**



Vermond, R.A. et al. J Am Coll Cardiol. 2015; 66(9):1000-7.

Bars represent the hazard ratio for incident atrial fibrillation (AF) of each individual risk factor in the multivariate model. The 95% confidence intervals (CIs) are shown under each bar. BMI = body mass index; HT = antihypertensive; MI = myocardial infarction.

Cardiovascular Health Study (inclusion from 1989 to 1993; last evaluation for AF in 1996) (6), the Atherosclerosis Risk in Communities study (inclusion from 1987 to 1989; follow-up until 1998) (7), and the Rotterdam Study (inclusion from 1990 to 1993; follow-up until 1999) (25)—followed their participants up to the 21st century, except the Framingham Heart Study (inclusion from 1948 to 1971; follow-up until 2008) (4,5), and the Women's Health Initiative (inclusion from 1994 to 1998; follow-up until 2007) (21). Our AF incidence rate is comparable to the incidence rates described in those older, and predominantly U.S.-based cohort studies (range, 3.3 to 19.2 per 1,000 person-years) (5–8,25). This is an interesting finding because improvements are continuously made in the treatment of cardiovascular risk factors for AF, including hypertension, coronary heart disease, and heart failure (11–13). Whereas improved treatment of cardiovascular diseases may reduce the risk of development of AF, increased life expectancy and changes in lifestyle such as inactivity and obesity may increase the incidence of AF. Together, these factors may have resulted in an AF incidence in the present study that is comparable to that of older studies.

COMORBIDITIES ASSOCIATED WITH INCIDENT AF. Most data on comorbidities associated with AF in the general population have been obtained from old U.S. cohorts that started inclusion before the introduction of contemporary treatments for myocardial infarction, hypertension and heart failure, and increasing availability of diagnostic tests, and changing lifestyle (11–13,26).

Associations of advancing age, male sex, hypertension, coronary heart disease, valve disease, heart failure, and diabetes mellitus with incident AF have been well established (4,6,7,21,25). In the present contemporary Dutch cohort, we found similar associations of well-established risk factors. In addition, obesity was an important contributor to AF risk. In a report from the third Atrial Fibrillation Competence NETwork/European Heart Rhythm Association

TABLE 3 **Incidence Rates of Cardiovascular Events, Heart Failure, and All-Cause Mortality per 1,000 Person-Years**

	Incidence Rate per 1,000 Person-Years (95% CI)		
	Incident AF (n = 265)	No AF (n = 8,000)	Hazard Ratio (95% CI)
Cardiovascular events*	20.59 (14.84–28.64)	10.13 (9.43–10.87)	1.97 (1.24–3.13)
Cerebrovascular events	5.53 (3.26–9.46)	2.42 (2.10–2.79)	2.23 (0.99–5.00)
Cardiac events	14.58 (10.05–21.21)	7.54 (6.95–8.19)	1.88 (1.12–3.16)
Peripheral events	1.63 (0.66–4.17)	0.72 (0.56–0.94)	2.20 (0.52–9.37)
Heart failure	18.14 (13.19–25.01)	2.91 (2.55–3.31)	6.01 (2.83–12.76)
LVEF <40%	12.75 (8.72–18.68)	1.99 (1.70–2.33)	5.79 (2.40–13.98)
LVEF >50%†	4.90 (2.69–9.02)	0.85 (0.67–1.08)	4.80 (1.30–17.70)
All-cause mortality	28.96 (23.05–36.42)	6.84 (6.28–7.44)	4.14 (2.64–6.51)

*Composite of cardiovascular events; some participants had multiple events. †Six participants with heart failure had an LVEF of 41% to 49%. To ensure a clear distinction between both systolic and diastolic heart failure, these participants are not shown in the table.

LVEF = left ventricular ejection fraction; other abbreviations as in Tables 1 and 2.

TABLE 4 Association of Incident AF* With Outcomes

	Hazard Ratio (95% CI)	p Value
Cardiovascular events		
Model 1	2.45 (1.34–4.49)	0.004
Model 2	2.24 (1.06–4.75)	0.035
Heart failure		
Model 1	6.11 (3.32–11.23)	<0.001
Model 2	4.52 (2.02–10.09)	<0.001
All-cause mortality		
Model 1	3.79 (2.34–6.14)	<0.001
Model 2	3.02 (1.73–5.27)	<0.001

*Time-varying covariate. Model 1: adjusted for age and sex. Model 2: adjusted for age, sex, prevalent heart failure, antihypertensive drug use, diabetes, previous stroke, previous myocardial infarction, peripheral artery disease, and N-terminal prohormone of brain natriuretic peptide.

Abbreviations as in Table 1 and 2.

consensus conference published in 2011 (12), BMI was considered a less-validated risk factor for AF. However, with a 45% increased risk of AF with every 5 points of BMI increase, the present study supports the notion that BMI should be regarded as a validated risk factor for AF.

Obesity often coexists with other cardiovascular risk factors and diseases (e.g., diabetes, metabolic syndrome, and sleep apnea syndrome). However, obesity by itself may also induce AF (21,27). Animal models of obesity showed the induction of cardiac ectopic fat and fat infiltration of the local atrial myocardium, potentially a novel substrate specific to obesity (28). Importantly, obesity is a modifiable risk factor, and it was shown that strict weight reduction reduced the AF burden (29). The population-attributable risk of obesity in this study provides an indication that a 9% reduction of incident AF could be achieved when the risk factor obesity was completely eliminated.

AF-RELATED CARDIOVASCULAR EVENTS, HEART FAILURE, AND MORTALITY. The present analysis confirms the association of AF with adverse outcomes, including cardiovascular events, heart failure, and all-cause mortality. Treatment of AF has significantly changed in the past decade. The most important change has been systematic use of oral anticoagulation in persons at risk for stroke (11). Although the overall event rates were lower in the present contemporary cohort, the associations with outcome were similar as previously described. The lower rates of cardiovascular events, heart failure, and all-cause mortality may be caused by improved treatment modalities. However, incident AF was still associated with a 2-fold increase of cardiovascular events including stroke, a 5-fold increased heart failure risk, and a 2-fold increased risk of all-cause mortality, largely similar to associations found previously (23,24). Despite the important improvements in oral anticoagulation reducing the risk of stroke (30–32), the risk of heart failure and the risk of all-cause mortality associated with AF are still high (24). Next to stroke prevention, more focus on prevention of heart failure and mortality in patients with AF seems important in the years to come, to improve prognosis of patients with AF further.

STUDY STRENGTHS AND LIMITATIONS. Strengths of our study are the contemporary cohort, the detailed clinical assessment, the long and contemporary follow-up period, and the robust validation of cardiovascular events, including AF. However, there are limitations, mainly resulting from the observational design of this community-based cohort study. We may have overlooked asymptomatic paroxysmal AF because we had no continuous ECG recordings (33). Moreover, given that a cardiovascular event was attributed to AF only when AF was diagnosed before the event occurred, the present event rates may be underestimated. Stroke was defined using ICD codes for occlusion or stenosis of the precerebral or cerebral arteries; no direct evaluation for stroke was performed. Data on obstructive sleep apnea were not available. Although treating physicians were informed about the presence of AF or other undiagnosed cardiovascular diseases, treatment was left to the discretion of the physician.

CONCLUSIONS

Results of our contemporary community-based study from the Netherlands confirm that although important progress in treatment of cardiovascular disease is continuously being made, the incidence of AF has not dramatically changed over the years. Obesity has become a major risk factor for incident AF. Whereas overall cardiovascular event rates were lower in the present study, incident AF still doubles the cardiovascular event risk and the all-cause mortality risk and increases the heart failure risk 5-fold. Identification and improved treatment of reversible risk factors for incident AF, and prevention of heart failure and mortality, may prevent AF and improve the prognosis of this arrhythmia.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Despite considerable progress in management of cardiovascular disease, the incidence of AF has not decreased, and this common rhythm disturbance is associated with adverse cardiovascular outcomes, including heart failure and stroke. In addition to well-established factors, obesity has become a risk factor for AF.

TRANSLATIONAL OUTLOOK: More research should be directed toward understanding the roles of weight reduction and lifestyle modification in prevention of AF.

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KEY WORDS atrial fibrillation, comorbidities, epidemiology, heart failure, mortality, outcome